induction was altered. Blocking FGF signaling for a prolonged time period significantly reduces expression of lung and liver markers but has only modest effects on the pancreas. Importantly, markers of foregut progenitors are not significantly disrupted with these treatments. Thus, we have found that the high doses of FGF needed to induce lung and liver are achieved at least partially through prolonged FGF signaling to the foregut progenitors. Additionally, it appears that multiple branches of the FGF signaling pathway are necessary for foregut organ induction and proliferation. In the future, it will be important to determine what targets of FGF are activated in the foregut precursors for specific foregut organ lineages and how the FGF signal is coordinated with signals from the Wnt and BMP pathways, which also play important roles in the developing endoderm.

doi:10.1016/j.ydbio.2011.05.409

Program/Abstract #448
The role of Foxi3 in otic placode induction
Ryan Mayle[a], Takahiro Ohyama[b], Renee Edlund[a], Hongyuan Zhang[a], Andrew Groves[a]
[a]*Houston, TX, USA*
[b]*Los Angeles, CA, USA*

The inner ear develops from the otic placode, an ectodermal thickening that is induced by FGF signaling and gives rise to the cochlea and vestibular system of the inner ear. Development of the inner ear begins at the end of gastrulation, when the otic placode is induced from the pre-placodal region, an area of ectoderm between the neural plate and early epidermis which gives rise to the cranial sensory placodes. We have previously shown that only ectoderm in the pre-placodal region (PPR) can be induced to become otic placode in response to FGF signals. However, what makes PPR cells uniquely competent to respond to FGF is unknown. The PPR is marked by expression of several transcription factors, such as Eya2, Six1, and Foxi3. In contrast to other PPR genes, we have recently shown that Foxi3 is necessary for otic development, as Foxi3 null mice completely lack inner ears. Initial observations show that the otic placode is not induced in Foxi3 nulls, as indicated by a lack of Pax2 expression, the earliest ear marker in mice. We hypothesize that Foxi3 may be a competence factor required for otic placode induction. We are assessing the effect of loss of Foxi3 in both mouse and chick embryos. We are currently studying the expression of PPR and early ear markers in Foxi3 mutant mice to determine when ear development fails. This may be at the level of FGF competence, PPR defects, or at another point during the molecular sequence of placode induction. In addition to the mouse experiments, we are using Foxi3 knockdown in early chick embryos to further elucidate Foxi3's role in conferring FGF competence in otic induction in vivo and in vitro.

doi:10.1016/j.ydbio.2011.05.410

Program/Abstract #449
Patterning of the vertebrate hindbrain: A computational approach
Yassine Bouchoucha, Juergen Reingruber, Johan Le Men, Pascale Gilardi-Hebenstreit, David Holcman, Patrick Charnay
Institute of Biology of the Ecole Normale Supérieure (IBENS), Paris, France

Patterning of the vertebrate hindbrain involves segmentation into 7 territories called rhombomeres. Odd rhombomeres (r3 and r5), which specifically express the transcription factor gene krox20, alternate with even-numbered, Krox20-negative rhombomeres. Regulation of Krox20 expression is key to determine the relative sizes of the rhombomeres, and includes two steps: initiation via the activation of initiator enhancers B and C, and autoregulation through enhancer A. FGF signalling plays a crucial role during segmentation, regulating the size of r3 and r5 through control of krox20 transcription. The mechanism underlying this regulation is still largely unknown. We have shown that FGFs control enhancers B and C, but not A. FGFs could control the number of krox20 + cells by regulating the initial level of krox20, thus determining if a cell can reach a threshold to permanently activate the autoregulatory loop and become krox20-positive. This mechanism would rely on a bistable system where a variable input controls the fate-determining autoregulation phase. Our goal is to use quantitative analyses in zebrafish to understand how transcription at the cellular level impacts cell-fate decisions. We have built a stochastic model to describe the system at the molecular level, where the number of krox20 molecules is a variable of initiator and autoregulatory element activity. To validate the model we designed an experimental setup allowing the control of krox20 input and measurement of the output of the autoregulatory loop in zebrafish embryos. Once validated, the model will incorporate additional regulations, e.g. the hoxb1-mediated inhibition of krox20 expression, thus providing a more comprehensive view of hindbrain segmentation.

doi:10.1016/j.ydbio.2011.05.411

Program/Abstract #450
Nr2f2 modulates FGF signaling to pattern rhombomere territories in the zebrafish hindbrain
Crystal E. Love[a], Victoria Prince[b]
[a]*University of Chicago Developmental Biology, Chicago, IL, USA*
[b]*The University of Chicago, Chicago, IL, USA*

The goal of this project is to determine the role of the Nuclear receptor subfamily 2, group F (nr2f) orphan nuclear receptor genes in patterning the vertebrate hindbrain using zebrafish as a model. The nr2f orphan receptor genes, also known as COUP-TF in mammals, are members of the steroid/thyroid hormone receptor superfamily, and are highly expressed in the developing CNS in vertebrates. Consistent with previous reports we find that the expression pattern of one member of this gene family, nr2f2, is localized to specific regions of the forebrain and hindbrain. The hindbrain is segmented into a series of 7 rhombomeres, and nr2f2 transcripts show graded rhombomere-specific expression levels in the hindbrain, suggesting this gene may play a role in rhombomere specification or regionalization. Proper patterning of the hindbrain requires FGF signaling from the midbrain-hindbrain boundary and rhombomere 4, as well as RA signaling from the posterior. We show that although these signaling pathways are not required for nr2f2 transcription, they are nevertheless sufficient to negatively regulate nr2f2 transcription. Exogenous RA signals abolish nr2f2 expression in the hindbrain, whereas FGF signaling functions to suppress nr2f2 expression in the midbrain. Additionally, we have used a morpholino knockdown approach to study the function of nr2f2. Knockdown of Nr2f2 results in disorganization of rhombomere territories and a decrease in FGF signaling within the hindbrain. These studies suggest that nr2f2 is involved in the interpretation and/or maintenance of complex FGF and retinoid signals within the hindbrain, and ongoing studies will test these hypotheses.

doi:10.1016/j.ydbio.2011.05.412

Program/Abstract #451
Sox21 is the maintenance factor for neural progenitors
Niteace C. Whittington, Doreen D. Cunningham, Elena S. Casey
Georgetown University Biology, Washington, DC, USA